CLAIMS

1. A method for the early detection of a flaviviral infection, characterized in that it comprises detecting the NS1 nonstructural glycoprotein of a flavivirus in a biological sample, throughout the duration of the clinical phase of the infection, by an immunological method using at least two antibodies, which may be identical or different,

- the first antibody or antibody for capturing the NS1 glycoprotein consisting of antibodies chosen from the group consisting of:
- polyclonal antibodies preselected by immunocapture on the NS1 protein of said flavivirus, in the hexameric form, and

- mixtures of anti-NS1 monoclonal antibodies preselected for their high affinity for the NS1 protein of said flavivirus, in the hexameric form, said monoclonal antibodies then being purified,

- the second antibody or revelation antibody being chosen from the group consisting of:

- polyclonal antibodies directed against the NS1 protein in the hexameric form, and

- a mixture of monoclonal antibodies directed against a NS1 protein in the hexameric form.

2. The detection method as claimed in claim 1, characterized in that the flaviviral infection is an infection with the dengue virus.

3. The detection method as claimed in either of claims 1 and 2, characterized in that the first antibody is attached to a suitable solid support

and the second antibody is optionally conjugated to a suitable label.

4. The detection method as claimed in claim 3, characterized in that when the second antibody is not conjugated to a label, its binding to the NS1 protein attached to the solid support is then detected with a third antibody, conjugated to a suitable label.

5. The detection method as claimed in claim 4, characterized in that the third antibody is conjugated to an enzyme.

6. The detection method as claimed in claim 5, characterized in that:

- the first antibody, or capture antibody, consists of mouse polyclonal antibodies selected by immunocapture on the NS1 protein of the dengue virus, said protein being in the hexameric form, and

- the second antibody, or antibody for detecting the presence of NS1 in the biological sample to be analyzed, consists of polyclonal antibodies from a rabbit immunized with the NS1 protein of dengue virus serotype 1, said protein being in the hexameric form, the attachment of said second antibody being revealed with a third antibody, consisting of antibodies conjugated to peroxidase and directed against the second antibody.

7. A boxed set for the early diagnosis of a flaviviral infection, characterized in that it comprises:

- at least one capture antibody and at least one revelation antibody as defined in any one of claims 1 to 6,

- at least one positive control consisting of the NS1 protein of a flavivirus and/or of various serotopes depending on the flavivirus, said protein being in the hexameric form, and

- at least one negative control consisting of a normal human serum.

8. The boxed set for diagnosis as claimed in claim 7, characterized in that said NS1 protein is obtained from a culture supernatant either from infected mammalian cells or from mammalian cells transfected with a recombined plasmid comprising the gene of the NS1 protein of a flavivirus or a fragment of said gene or a fragment of the flaviviral genome, said fragments being capable of expressing all or part of the NS1 protein.

9. The boxed set for the early diagnosis of a flaviviral infection as claimed in either of claims 7 and 8, characterized in that the NS1 protein is that of the dengue virus.

10. The boxed set for the early diagnosis of a flaviviral infection as claimed in either of claims 8 and 9, characterized in that said plasmid was deposited with the Collection Nationale de Cultures et de Microorganismes [National collection of cultures and microorganisms] held by the Institut Pasteur under the number I-2220, dated June 7, 1999.

11. A method for purifying the NS1 protein of a flavivirus, in the hexameric form, from a culture supernatant either of infected mammalian cells or of mammalian cells transfected with a recombined plasmid comprising the gene of the NS1 protein or a fragment of said gene or a fragment of the

flaviviral genome, said fragments being capable of expressing the NS1 protein, characterized in that, prior to the purification of the NS1 protein using conventional techniques, it comprises a step for separating the soluble form of the NS1 protein from the microparticulate form of said protein, by treatment with a precipitating agent and then by centrifugation.

12. An immunogenic composition, characterized in that it comprises, as the active principle, the NS1 protein of a flavivirus, in the hexameric form, optionally associated with other proteins, in combination with at least one pharmaceutically acceptable vehicle.

13. The immunogenic composition as claimed in claim 12, characterized in that it comprises at least one mixture of the NS1 proteins in the hexameric form corresponding to the various dengue virus serotypes.

14. The use of the NS1 protein in the hexameric form, or of a system for the expression thereof, for preparing an immunogenic composition capable of inducing the production of antibodies *in vivo*.

15. The use of at least one monoclonal anti-NS1 antibody having a high affinity for the NS1 protein in the hexameric form, said form being nondegraded, said monoclonal antibodies then being purified and modified, for manufacturing a medicinal product capable of inducing passive immunization.

16. The use of the NS1 protein in the hexameric form, said form being nondegraded, for selecting *in vitro* specific anti-NS1 antibodies able to

diagnose an infection with a flavivirus, at an early stage.

17. An immunogenic composition, characterized in that it comprises an active principle selected from the group consisting of:

- a polynucleotide capable of expressing all or part of the NS1 protein of the dengue virus, whatever its serotype,

- an expression system comprising at least one promoter capable of expressing, in the host into which it is injected, a DNA encoding the NS1 protein of the dengue virus, whatever its serotype, said gene expressing said protein,

in combination with at least one pharmaceutically acceptable vehicle.

18. A method for expressing a polynucleotide encoding the NS1 protein of a dengue virus, characterized in that it comprises the expression of a polynucleotide as defined in the sequence SEQ ID No. 1, associated with a promoter for said polynucleotide, in suitable eukaryotic cells.

19. The method for purifying the NS1 protein as claimed in claim 11, characterized in that the flavivirus is a dengue virus, whatever its serotype.

20. The method for purifying the NS1 protein as claimed in claims 11 and 19, characterized in that the flavivirus is a dengue virus serotype 1.